REMARKS

Claims 1-17 were pending in this application. The Applicant has cancelled claims 1-17 without prejudice to prosecuting these same, or similar claims, in subsequently filed applications.

The Applicant has amended the Specification by inserting a priority claim, as provided by 35 U.S.C. § 120, originally recited in paragraph 16 of the "New Application Transmittal" filed with the instant application.

Finally, the Applicant has added claims 18-23 in the instant correspondence. The Examiner made the following rejections:

(1) The Examiner rejects claims 1-5 and 9 under the judicially created doctrine of obviousness-type double patenting.

(2) The Examiner rejects claims 1-17 under 35 U.S.C. 102(b).

(3) The Examiner rejects claims 1-17 under 35 U.S.C. 103(a).

The Applicant believes the present amendments, and the following remarks, traverse the Examiner's rejections. These remarks are presented in the same order as they appear above.

1. "Obviousness" Type Double Patenting Is Not Applicable

The Examiner has rejected claims 1-5 and 9, under alleged obviousness type double patenting, in view of claims 1-3 in U.S. Patent 6,685,951. Moreover, the Examiner *provisionally* rejects, under alleged obviousness type double patenting, claims 1-8 and 14 in view of copending application Serial No.: 09/899,412.

The Applicant disagrees. In view of the new claim set, introduced in the instant correspondence, the Applicant respectfully requests the Examiner reconsider the pending obviousness type double patenting rejection as set out in the pending Office Action.

2. The Claims are Not Anticipated

The Examiner has rejected claims 1-17 under 35 U.S.C. 102(b) as anticipated by U.S. Patent 6,043,244 to Caruso. The Applicant respectfully disagrees. The MPEP states that "to anticipate a claim, the reference must teach *every* element of the claim." Emphasis added, MPEP § 2131. Additionally, "[t]he rule is that the burden of persuasion is on the PTO to show why the applicant is not entitled to a patent." *In re Epstein*, 31 USPQ2d 1817, 1825 (Fed. Cir. 1994) (Plager, J. joined by Cowen, J., concurring.) (citing to *In re Oetiker*, 977 F.2d 1443, 24 USPQ2d 1443 (Fed. Cir. 1992) (Plager, J., concurring); *In re Warner*, 379 F.2d 1011, 1016, 154 USPQ 173, 177 (CCPA 1967), *cert. denied*, 389 U.S. 1057(1968)). "[T]he examiner bears the initial burden, on review of the prior art or on any other ground, of presenting a *prima facie* case of unpatentability. If that burden is met, the burden of coming forward with evidence or argument shifts to the applicant . . . . If examination at the initial stage does not produce a *prima facie* case of unpatentability, then without more the applicant is entitled to grant of the patent." *In re Oetiker*, 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992).

By the Examiner's own admission, the Caruso reference does not teach the claimed invention:

> "Caruso teaches a method treating migraines wherein dyhydroergotamine (sic) is administered with an antimigraine-potentiating amount of an NMDA receptor antagonist." Office Action dated 06/17/2004, p. 3.

Thus, the cited prior art reference *requires* the inclusion of a NMDA receptor antagonist in all disclosed formulations. In view of this distinction, and in order to advance the Applicant's business interests with respect to particular embodiments while reserving the right to prosecute similar or identical claims in the future, the Applicant has cancelled pending claims 1-17 and added claims 18-23.

While no new matter has been added, these new claims (e.g. 18-23) recite a formulation comprising dihydroergotamine and a steroid.[1] Steroids may not be categorized as an NMDA receptor agonist. Caruso is silent on the co-formulation of dihydroergotamine with a steroid (or the supplementation of a dihydroergotamine and NMDA receptor antagonist with a steroid) and, therefore, Caruso may not anticipate the invention as claimed. In view of the above, the Applicant respectfully submits the pending rejection, under 35 U.S.C. 102(b), need be withdrawn.

3. The Claims Are Not Obvious

A. The Examiner Fails to Make a *Prima Facie* Case of Obviousness

The Examiner is reminded that a *prima facie* case of obviousness requires citation to a combination of references which (a) disclose the elements of the claimed invention, (b) suggests or motivates one of skill in the art to combine the elements to yield the claimed combination, and (c) provides a reasonable expectation of success should the claimed combination be carried out. Failure to establish any one of these three requirements precludes a finding of a *prima facie* case of obviousness, and, without more, entitles Applicants to allowance of the claims in issue. *See, e.g., Northern Telecom Inc. v. Datapoint Corp.*, 15 U.S.P.Q.2d 1321, 1323 (Fed. Car. 1990).

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[1] Support for the co-formulation of DHE with steroids may be found, in the application as filed, at page 24, ll. 7-11.

The Applicants respectively submit the Examiner has failed to establish a *prima facie* case of obviousness.

i. The Examiner Must Point to Evidence

The requirement that the Examiner make a showing of a suggestion, teaching or motivation is "an essential evidentiary component of an obviousness holding." *C.R. Bard, Inc. v. M3 Sys. Inc.*, 157 F.3d 1340, 1352 (Fed. Car. 1998). There are three sources for this evidentiary component: the prior art references themselves, the knowledge of one of ordinary skill in the art, or, in some cases, from the nature of the problem to be solved. *Pro-Mold & Tool Co. v. Great Lakes Plastics, Inc.*, 75 F.3d 1568, 1573 (Fed. Car. 1996). The suggestion most often comes from the teachings of the pertinent references. *In re Rouffet*, 149 F.3d 1350, 1359 (Fed. Car. 1998). Nonetheless, regardless of the source of the requisite evidence, the Examiner's showing "must be clear and particular, and broad conclusory statements...standing alone, are not 'evidence'." *In re Dembiczak*, 175 F.3d 994, 1000 (Fed. Car. 1999).

It is the Examiner's burden to present "evidence" and this showing must be "clear and particular." *Id.* Importantly, since an Examiner is NOT one skilled in the art (under the law), the Examiner's opinion on what one skilled in the art might believe does not count. *In re Rijckaert*, 9 F.3d 1531, 28 U.S.P.Q.2d 1955, 1956 (Fed. Car. 1993) ("[T]he examiner's assumptions do not constitute the disclosure of the prior art"). Of course, if the Examiner has knowledge of relevant facts which are used to make the rejection, the Examiner is free to use those facts - but only if submitted in the form of an affidavit. *See* 37 C.F.R. § 1.107(b). In the present case, the Examiner has submitted no such affidavit.

Indeed, the Examiner has provided only an opinion and perfunctory, conclusory statements - this is not the requisite "evidence" needed to support an obviousness rejection. The Examiner simply asserts that:

> "At the time the invention was made, it would have been obvious to a person of ordinary skill in the art to use any form of DHE is (sic) a method of treating migrane. .... One of

> ordinary skill in the art would have been motivated to do this to provide a method treating migraines that is effective ...".
> Office Action dated 06/17/04, p. 4.

The Examiner does not explain the relationship between the cited reference and the pending claimed methods for the treatment of migraines with the administration of a formulation comprising dihydroergotamine and a steroid. Moreover, without the requisite affidavit, the Examiner's assertions of what is known by "one of ordinary skill in the art" merits no consideration in the evaluation of the invention as claimed *vis-a-vis* 35 U.S.C. 103(a).

ii. Caruso Teaches Away From The Invention As Claimed

As discussed above, the pending claims teach (in part) the treatment of migrane with the administration of dihydroergotamine and a steroid. In contrast, Caruso teaches that,

> ". . .in addition to the antimigraine drug and antimigraine- potentiating amount of an NMDA receptor blocker or substance that blocks a major intracellular consequence of NMDA receptor activation, the therapeutic composition herein can contain at least one other pharmacologically active substance e.g., caffeine (a stimulant), an antiemetic drug such as metoclopramide, domperidone, belladonna alkaloids and phenothiazines such as chlorpromazine, prochlorperazine, and promethazine, a non-narcotic analgesic, e.g., acetaminophen or a *nonsteroidal anti-inflammatory* drug such as aspirin, diclofenac, diflusinal, etodolac, fenbufen, fenoprofen, flufenisal, flurbiprofen, ibuprofen, indomethacin, ketoprofen, ketorolac, meclofenamic acid, mefenamic acid, nabumetone, naproxen, oxaprozin, phenylbutazone, piroxicam, sulindac, tolmetin, zomepirac, and the like." U.S. Patent 6,043,244, Col. 8, ll. 11-27. (emphasis added).

Despite providing a laundry list of supplemental nonsteroidal anti-inflammatory compounds, Caruso is conspicuously silent on co-formulating *steroids* with any of the anti-migraine formulations taught in the '244 patent. Indeed the significant side effects,[2] associated with systemic administration of steroids, may explain Caruso's decision to exclude steroids from the teachings in the '244 patent. The Applicant,

[2] e.g. hypertension, gastritis, and myopathy.

however, appreciates that steroids have beneficial therapeutic properties[3] (*vis-a-vis* the treatment of migraine) and that sublingual administration of steroids allows for a prospective reduction of dose (and thereby reduction of side effects and toxicities) given: i) the direct transmucosal delivery into the bloodstream and ii) a reduction of the first pass effect associated with enteral administration. Glucocorticoid, for example, (in part) stimulate gluconeogenesis and inhibit the uptake of glucose from muscle and adipose tissue. These physiological effects would be desirable in supplementing the action of DHE in methods for the treatment of migraine.

Caruso, therefore, teaches away from the claimed embodiments of the present invention and fails to provide any motivation for one skilled in the art to recapitulate the same. Given the '244 patent to Caruso would likely lead an investigator in a direction divergent from the path taken by the Applicant, the '244 patent may not support a rejection under 35 U.S.C. 103. See, *Para-Ordnance Manufacturing v. SGS Importers International*, 37 USPQ2d 1237,1241 (Fed. Cir. 1995) (quoting *In re Gurley*, 31 USPQ2d 1130, 1131 (Fed. Cir. 1994)).

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[3] The Applicant also notes there is no obligation to described the underlying mechanism of the claimed methods and the following remarks in no way limit the scope of the invention as claimed.

CONCLUSION

The Applicant submits the amendments and arguments set forth above traverse the Examiner's rejections and, therefore, request that these rejections be withdrawn and the pending claims be passed to allowance. Should the Examiner believe a telephone interview would aid in the prosecution of this application, the Applicant encourages the Examiner to call the undersigned collect at 617.984.0616.

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